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Monica G. Marcu

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TWO PRUDENTIAL PLAZA, SUITE 4900

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CHICAGO, IL 60601-6731

EXAMINER

LE, EMILY M

ART UNIT

PAPER NUMBER

1648

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

09/936,449

Applicant(s)

MARCU ET AL.

Examiner

Emily Le

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 09/13/2006+12/21/2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
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| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of Claim(s)***

1. Claims 2 and 14-23 are cancelled. Claims 1 and 3-13 are pending and under examination.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 3-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

In response to the rejection, Applicant submits that the specification provides adequate written support for the term "about". To support Applicant's argument, Applicant cited line 34, page 15 of the specification.

Applicant's submission has been considered, however, it is not found persuasive. Line 34, page 15 discloses "a concentration of about .08 mM novobiocin". This cited passage adequate sets for adequate written description for the variable concentration of novobiocin, whereby the variable concentration is "about .08 mM". However, this cited passage does not set forth adequate written description for the recitation "about 100 mg/kg".

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As set forth in the previous office action, claim 1 has been amended to require the amount to be administered to "about 100 mg/kg", and at an interval of "at least once per day for about 5 days".

To show support for the cited recitations, Applicant cited lines 1-24 on page 16. Lines 1-24 on page 16 provide the following: "...normal C57B16 mice received intraperitoneal injections (100 mg/kg) of novobiocin (a coumarin antibiotic) at 12 hour interval for 5 days".

Accordingly, the limitations 100 mg/kg and 12 hour interval for 5 days is fully supported by the passage cited by Applicant, and as recaptured above by the Office. However, the cited passage does not express, implicit or inherent, an administration dosage amount of "about 100 mg/kg", and regimen of "at least once per day for about 5 days", as currently recited in the claims. In the instant, a difference in scope exists between the dosage amount and frequency of the treatment regimen disclosed in the original specification and those recited in the current claims. Thus, in view of this difference in scope, the claims are rejected under 35 U.S.C 112, 1<sup>st</sup> paragraph for the absence of adequate written description for the cited recitations.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3 and 5-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Eder et al,<sup>1</sup> as evidenced by Marcu et al.<sup>2</sup>

In response to the rejection, Applicant submits that Eder et al. does not anticipate the claimed invention. Applicant submits that Eder et al. teaches the administration of another compound, alkylating agents that materially affect the basic and novel properties of the claimed invention, wherein the inhibition of binding of a chaperone protein with its client protein is the basic and novel properties.

Applicant's submission has been considered, however, it is not found persuasive. Arguments cannot take the place of evidence. In the instant case, Applicant has not provided any evidence showing that the alkylating agents administered by Eder et al., along with the coumarin (novobiocin) affects the basic and novel characteristic of the claimed invention. Additionally, it is more likely than not that the alkylating agent works with novobiocin in inhibiting the binding of chaperone protein to its client protein. Additionally, Eder et al. teaches the synergistic use of the novobiocin with alkylating agents. Moreover, Eder et al. does not teach the use of the alkylating agents to interfere with novobiocin.

Additionally, Applicant it is note that Applicant submits that the 10 day treatment period does not read on "about 5 days".

Applicant's submission has been considered, however, it is not found persuasive. As stated in the previous office action, because Applicant has not set forth a rigid

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<sup>1</sup> Eder et al. Effect of novobiocin on the antitumor activity and tumor cell and bone marrow survivals of three alkylating agents. Cancer Research, 1989, Vol. 49, Issue 3, 595-598.

guideline regarding what Applicant regards as “about 5 days”. In the absence of such guideline, the Office continues to interpret 10 days to be “about 5 days.”

As previously presented, the claims are directed to a method of inhibiting the binding of a chaperon protein with its client protein or client polypeptide in a mammal, wherein the method comprises contacting Hsp90 with coumarin or a coumarin derivative, whereby about 100 mg/kg of coumarin or coumarin derivative is administered to the mammal at least once per day for about 5 days.

Claim 3, which depends on claim 1, requires the coumarin or coumarin derivative to be a coumarin antibiotic. Claim 5, which depends on claim 3, defines the coumarin antibiotic as novobiocin. Claim 6, which depends on claim 1, also limits the coumarin or coumarin derivative to novobiocin. Claim 7, which depends on claim 6, requires novobiocin to bind to the carboxyl-terminal region of Hsp90. Claim 8, which depends on claim 1, defines the client protein or client polypeptide as tyrosine or serine/threonine kinase. Claim 9, which depends on claim 8, limits the tyrosine kinase to p185<sup>erbB2</sup> or p60<sup>v-src</sup>. Claim 10, which depends on claim 8, limits the serine/threonine kinase to Raf-1. Claim 11, which depends on claim 1, defines the client protein or client polypeptide as mutated p53 protein. Claim 12, which depends on claim 1, expresses that the client protein or client polypeptide to be inactive subsequent to binding of Hsp90 to the coumarin or coumarin derivative. Claim 13, which depends on claim 12, specifies that the client protein or client polypeptide be degraded.

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<sup>2</sup> Marcu et al. The heat shock protein 90 antagonist novobiocin interacts with previously unrecognized ATP-binding domain in the carboxyl terminus of the chaperone. The Journal of Biological Chemistry, 2000, Vol. 275, No. 47, 37181-37186.

In the instant, Eder et al. teaches a method comprising the administration coumarin or coumarin derivative to a mammal. The coumarin derivative that Eder et al. administered to the mammal is novobiocin, a coumarin antibiotic. [Abstract] The amount of novobiocin that Eder et al. administered to the mammal includes 50 mg/kg and 100mg/kg to the mammals. [Tumor Growth Delay Experiments segment under the Materials and Methods section disclosed on page 595.] Eder et al. teaches the administration novobiocin once daily on days 6 through 15 post tumor implantation. In the instant, the frequency in which Eder et al. administered novobiocin is once daily for 10 days; wherein the 6th day post tumor implantation serves as the first day in which the first dose of novobiocin is administered and the 15th day post tumor implantation serves as the 10th day in which the last dose of novobiocin is administered to the mammal. Eder et al. notes that the administration of novobiocin inhibits cellular proliferation, particularly cancer.

In summary, Eder et al. teaches a method comprising the administration coumarin or coumarin derivative to a mammal. The amount in which novobiocin was administered to the mammal by Eder et al. is about 100 mg/kg. The frequency in which novobiocin is administered to the mammal by Eder et al. is at least once per day for about 5 days. In the instant, while the Office does note that the claims specifically recite "about 100 mg/kg" and "about 5 days"; however, in the absence of any guidance from specification for the extent of coverage the term "about" provides, the Office regards the 50 mg/kg and 100mg/kg, and the 10 day treatment period as being encompassed by recitations "about 100 mg/kg" and "about 5 days", respectively. Therefore, Eder et al.

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teaches a method comprising the administration coumarin or coumarin derivative to a mammal, wherein about 100 mg/kg of coumarin or coumarin derivative is administered to the mammal at least once per day for about 5 days, and whereby the coumarin or coumarin derivative is novobiocin.

Additionally, the Office notes that Eder et al. does not acknowledge that the administration of novobiocin inhibits the binding of Hsp90 with its client protein or client polypeptide. However, MPEP § 2112 [R-3] (I) provides the following:

“[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Thus, in accordance with the guidance provided by MPEP § 2112 [R-3] (I), Eder et al. does not need to appreciate or acknowledge that novobiocin inhibits the binding of Hsp90 with its client protein or client polypeptide to render the claimed invention unpatentable. In the instant, while the Office does appreciate the scientific explanation offered by Applicant, however, Applicant's discovery or appreciation of the mechanism of action in which novobiocin function in a mammal is not sufficient to render Applicant's discovery patentable. In all, Applicant's appreciation or discovery of an unknown property that is inherently present in the prior art does not make Applicant's claimed invention patentable.

Furthermore, it is clearly evident from the art that novobiocin inhibits the binding of Hsp90 with its client protein or client polypeptide. See the teachings of Marcu et al. Marcu et al. teaches that novobiocin antagonizes Hsp90 in vitro and in vivo by binding



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to the carboxyl terminus of Hsp90. [First sentence under the Discussion section disclosed on page 37185, and the title of the article.] Marcu et al. further teaches that the antagonizing activity of novobiocin against Hsp90 leads to the rapid destabilization of various Hsp90 client proteins, including Raf-1, p60<sup>v-src</sup>, and p185<sup>erbB2</sup> --all of which are tyrosine and serine/threonin kinases, and mutated p53. [First full paragraph disclosed on the right column of page 37181] Thus, Marcu et al. clearly evidenced that the administration of novobiocin, as Eder et al. teaches, inherently lead to the inhibition of binding of Hsp90 with client protein or client polypeptides. Additionally, Marcu et al. clearly evidenced that novobiocin inherently i) binds to the carboxyl-terminal region of Hsp90; ii) inhibits the binding of Hsp90 with its client proteins (Raf-1, p185<sup>erbB2</sup> and p60<sup>v-src</sup> -- all of which are tyrosine and serine/threonin kinases, and mutated p53); and iii) inactivates the client proteins since the chaperone protein (Hsp90) is no longer available to mediate the function of these client proteins; which in essence is the equivalent of degrading these proteins. Hence, in view of the evidence provided by Marcu et al., Eder et al. does teach a method of inhibiting the binding of Hsp90 with its client protein or client polypeptide in a mammal, wherein the method comprises contacting Hsp90 with novobiocin by administering about 100 mg/kg of novobiocin, for at least once per day for about 5 days to the mammal. Therefore, Eder et al. anticipates the claimed invention.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Civitico et al.,<sup>3</sup> as evidenced by Hu et al.<sup>4</sup>

In response to the rejection, Applicant submits that Civitico et al. does not teach, suggest or motivate a skilled artisan to reach each and every limitation of the claimed invention. Specifically, Applicant submits that Civitico et al. does not teach, suggest or motivate one of ordinary skill in the art to contact a chaperone protein with a coumarin or coumarin derivative, wherein about 100 mg/kg of coumarin or coumarin derivative is administered to a mammal at least once per day for about 5 days and, wherein the chaperone protein is a mammal.

Applicant's submission has been considered, however, it is not found persuasive. Contrary to Applicant's assertion, the suggestion and motivation to administer coumarin, novobiocin, to a mammal is clearly provided by Civitico et al. As provided in the previous office action, Civitico et al. teaches that novobiocin inhibits the replication of duck hepatitis B virus. Civitico et al. does not teach the administration of novobiocin to a mammal. However, Civitico et al. does suggest the use of novobiocin in the

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<sup>3</sup> Civitico et al. Antiviral strategies in chronic hepatitis B virus infection: II. Inhibition of duck hepatitis B virus in vitro using conventional antiviral agents and supercoiled-DNA active compounds. Journal of Medical virology, 1990, Vol. 31, 90-97.

management of chronic hepatitis B infection. [Abstract.] Hence it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to administer novobiocin to a mammal that is infected with hepatitis B virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to provide treatment for hepatitis B viral infection. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Civitico et al. demonstrates the antiviral activity of novobiocin against hepatitis B virus.

It is additionally noted that Applicant argues that Hu et al. does not compensate for the deficiencies of Civitico et al.

Applicant's submission has been considered, however, it is not found persuasive. Applicant is reminded that the instant obviousness rejection renders the claimed invention obvious over the teachings of Civitico et al., as **evidenced by** Hu et al. In the instant case, Hu et al. is evidence cited to demonstrate the inherent, chemical or mechanistic, property of novobiocin and Hsp 90.

As presented in the previous office action, the claims are directed to a method of inhibiting the binding of heat shock protein (Hsp) 90 with its client protein or client polypeptide in a mammal, wherein the method comprises contacting Hsp90 with coumarin or a coumarin derivative, whereby about 100 mg/kg of coumarin or coumarin derivative is administered to the mammal at least once per day for about 5 days.

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<sup>4</sup> Hu et al. Hsp90 is required for the activity of hepatitis B virus reverse transcriptase. Proc. Natl. Acad. Sci. USA, 1996, Vol. 93, 1060-1064.

In the instant case, Civitico et al. teaches that novobiocin inhibits the replication of duck hepatitis B virus. Civitico et al. does not teach the administration of novobiocin to a mammal. However, Civitico et al. does suggest the use of novobiocin in the management of chronic hepatitis B infection. [Abstract.] Hence it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to administer novobiocin to a mammal that is infected with hepatitis B virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to provide treatment for hepatitis B viral infection. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Civitico et al. demonstrates the antiviral activity of novobiocin against hepatitis B virus.

Furthermore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to determine the workable or optimal treatment protocol, including dosage amount, frequency of administration, and duration of the treatment for the mammal. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to treat the mammal of hepatitis B viral infection. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the determination of a workable or optimal treatment protocol is routinely practiced in the art.

Additionally, the Office notes that Civitico et al. does not acknowledge that the administration of novobiocin inhibits the binding of Hsp90 with its client protein or client

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polypeptide, hepatitis B virus reverse transcriptase. However, MPEP § 2112 [R-3] (I) provides the following:

"[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Thus, in accordance with the guidance provided by MPEP § 2112 [R-3] (I), *Civitico et al.* does not need to appreciate or acknowledge that novobiocin leads to the inhibits the binding of Hsp90 with hepatitis B virus reverse transcriptase to render the claimed invention unpatentable. In the instant, while the Office does appreciate the scientific explanation offered by Applicant, however, Applicant's discovery or appreciation of the mechanism of action in which novobiocin function is not sufficient to render Applicant's discovery patentable. In all, Applicant's appreciation or discovery of an unknown property that is inherently present in the prior art does not make Applicant's claimed invention patentable.

Furthermore, it is clearly evident from the art, *Hu et al.*, that novobiocin does inhibit the binding of Hsp90 with hepatitis B virus reverse transcriptase to promote its antiviral activity. *Hu et al.* teaches that hepatitis B viruses replicates through a reverse transcription pathway. *Hu et al.* also teaches that the hepatitis B virus reverse transcriptase relies on Hsp90 to mediate its function. Hence, *Hu et al.* teaches that Hsp90 is required for the activity of hepatitis B virus reverse transcriptase, and the hepatitis B virus reverse transcriptase is necessary for hepatitis B viral replication. In the instant, *Civitico et al.* teaches that hepatitis B viral replication is inhibited by

novobiocin. Thus, novobiocin would inherently inhibit the binding of Hsp90 with hepatitis B virus reverse transcriptase, which results in the antiviral activity, inhibition of duck hepatitis B virus replication, observed by Civitico et al.

8. Claims 1 and 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Eder et al., as evidenced by Marcu et al., as applied to claims 1 and 3 above, in view of Gormley et al.<sup>5</sup>

In response to the rejection, Applicant submits that Eder et al. does not anticipate the claimed invention. Applicant submits that Eder et al. teaches the administration of another compound, alkylating agents, that materially affect the basic and novel properties of the claimed invention, wherein the inhibition of binding of a chaperone protein with its client protein is the basic and novel properties.

Applicant's submission has been considered, however, it is not found persuasive. Arguments cannot take the place of evidence. In the instant case, Applicant has not provided any evidence showing that the alkylating agents administered by Eder et al., along with the coumarin (novobiocin) affects the basic and novel characteristic of the claimed invention. Additionally, it is more likely than not that the alkylating agent works with novobiocin in inhibiting the binding of chaperone protein to its client protein. Additionally, Eder et al. teaches the synergistic use of the novobiocin with alkylating agents. Moreover, Eder et al. does not teach the use of the alkylating agents to interfere with novobiocin.

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<sup>5</sup> Gormley et al. The interaction of coumarin antibiotics with fragments of the DNA gyrase B protein. *Biochemistry*, 1996, Vol. 35, 5083-5092.

Additionally, Applicant it is note that Applicant submits that the 10 day treatment period does not read on "about 5 days".

Applicant's submission has been considered, however, it is not found persuasive. As stated in the previous office action, because Applicant has not set forth a rigid guideline regarding what Applicant regards as "about 5 days". In the absence of such guideline, the Office continues to interpret 10 days to be "about 5 days."

As previously presented, claim 4, which depends on claim 3, which depends on claim 1, limits the coumarin or coumarin derivative to chlorobiocin or coumermycin A1.

The significance of Eder et al. and Marcu et al., as it pertains to claims 1 and 3, is provided above. As presented above, Eder et al. teaches a method of inhibiting the binding of Hsp90 with its client protein or client polypeptide in a mammal, wherein the method comprises contacting Hsp90 with novobiocin by administering about 100 mg/kg of novobiocin, for at least once per day for about 5 days to the mammal. The coumarin derivative that Eder et al. uses is novobiocin. Neither Eder et al. nor Marcu et al. teaches the use of chlorobiocin or coumermycin A1 as the coumarin derivative.

However, Gormley et al. teaches chlorobiocin, coumermycin A1 and novobiocin. Gormley et al. teaches that chlorobiocin, coumermycin A1 and novobiocin have close structural similarity among one another, and have similar utilities. [Figure 1] Gormley et al. also teaches that chlorobiocin, coumermycin A1 and novobiocin are coumarin antibiotics. [Abstract] Hence, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use any of these coumarin derivatives as functional alternatives for the other. One of ordinary skill in the art the

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time the invention was made would have been motivated to do so to inhibit the binding of Hsp90 with its client protein or client polypeptide in a mammal. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because these compounds are expected to have similar properties with one another.

### ***Conclusion***

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone



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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce R. Campell  
Supervisory Patent Examiner  
Art Unit 1648

/E.Le/

A handwritten signature in black ink, appearing to read "Bruce Campell", with a stylized, cursive script.

BRUCE R. CAMPELL, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600